JTL 13 (2) DECEMBER 2024
Page: 174-185

Contents list available at Jurnal Teknologi Laboratorium

JURNAL TEKNOLOGI LABORATORIUM

Journal Homepage: www.teknolabjournal.com
ISSN 2580-0191(Online) I ISSN 2338 – 5634(Print)

Original Research

OPEN ACCESS

Evaluation of hydrogel formulated with seaweed extract (Ulva lactuca) for incised wound healing in white rats (Rattus norvegicus)

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Abstract: Skin, as the largest organ in the human and animal body, serves as the main protection against various external factors such as sharp objects, extreme temperatures, chemicals, or physical trauma. This study aims to evaluate the effectiveness of seaweed (Ulva lactuca) extract-based hydrogel in accelerating incision wound healing in Rattus norvegicus rats. This experimental study used a post-test only controlled group design with six treatment groups: Ulva lactuca hydrogel 5%, 10%, 15%, positive control (Bioplasenton), negative control (wound without treatment), and rat group without treatment. Data were analyzed using ANOVA test. The results showed that Ulva lactuca hydrogel 5% gave the best results in accelerating wound healing. The wound diameter in the 5% group decreased significantly, from 15.3 cm on day 0 to 10.9 cm on day 3, 4.7 cm on day 6, and 2.36 cm on day 14. Histopathology results showed increased epithelialization, decreased inflammation, and increased collagen deposition in the 5% group compared with the control group. Quantitatively, the 5% hydrogel group achieved wound healing up to 30% faster than the positive control and 50% faster than the negative control. The 5% Ulva lactuca hydrogel proved to be most effective in accelerating wound healing by modulating inflammation and promoting tissue regeneration. This concentration provides an optimal balance between efficacy and safety, making it a potential alternative for wound therapy.

Keywords: Skin histopathology; hydrogel; Ulva lactuca; cut wounds

INTRODUCTION

Incisional wounds, or cuts, are linear breaks in the skin and underlying tissue that can lead to bleeding, loss of organ function, contamination, and cell death. The wound healing process involves three main phases: inflammation, proliferation and maturation[1]. In the inflammatory phase, neutrophils and macrophages in the wound area produce Reactive Oxygen Species (ROS) to kill pathogens[2]. The wound healing process consists of three phases: the inflammatory phase, proliferation phase and maturation phase. In the inflammatory phase, the injured tissue will attract neutrophils and macrophages. These cells will produce ROS (Reactive Oxygen Species) that affect the surrounding tissue[3].

The increased production of ROS (Reactive Oxygen Species) results in high oxygen in the wound healing process and plays a role in killing pathogens. However, excess ROS (Reactive Oxygen Species) can cause tissue damage due to an imbalance between prooxidants and antioxidants in cells. In this condition, it can disrupt cell function, prolong the inflammatory phase, and inhibit the proliferation process and collagen formation by fibroblasts, which ultimately interferes with the wound healing process[4].

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DOI: 10.29238/teknolabjournal.v13i2.536
Received 02 September 2024; Received in revised form 06 December 2024; Accepted 19 December 2024

To accelerate the wound healing process, efforts are needed to shorten the duration of the inflammatory phase. The use of plant extract-based hydrogel preparations can help accelerate the transition from the inflammatory phase to the proliferation phase, resulting in faster wound healing. Metabolite compounds such as flavonoids, terpenoids, alkaloids, saponins, triterpenoids, and tannins have an important role in modulating the inflammatory phase. Flavonoids work as anti-inflammatory agents by inhibiting the activity of cyclooxygenase and lipooxygenase enzymes, which play a role in the inflammatory pathway. In addition, flavonoids also reduce leukocyte accumulation in the wound area and inhibit the synthesis of prostaglandins from arachidonic acid through inhibition of cyclooxygenase enzymes. These mechanisms contribute to the accelerated resolution of inflammation, allowing the process of tissue regeneration to begin more quickly[5].

Hydrogel is one of the autolytic wound dressing methods that works by shedding necrotic tissue naturally by the body in sheet form. The use of hydrogels is increasingly in demand due to its various benefits, such as maintaining skin moisture, keeping the wound surface clean, protecting the wound from external exposure, and its ability to absorb exudates[6]. Hydrogels contain hydrophilic polymers that are able to absorb large amounts of water without damaging the material structure. In addition, the propylene glycol content in hydrogels helps the penetration of active ingredients, prevents evaporation, and provides a bacteriostatic effect[7].

Nowadays, various types of synthetic and herbal medicines are increasingly used in medicine to accelerate the wound healing process, both minor and severe wounds, as an alternative or complement to conventional medical therapy. The use of synthetic drugs is often based on in-depth scientific research regarding their active components and mechanism of action in the body, while herbal drugs, which are made from natural materials such as plants, are also widely utilized because they are considered safer with lower side effects, and have the potential to accelerate wound healing through various bioactive properties contained in them, such as antioxidants, antibacterial, and anti-inflammatory[8]. One herbal plant that is often utilized in traditional medicine in Indonesia is seaweed (Ulva lactuca), which is known to have various benefits as an antibacterial, antioxidant and anticoagulant[9]. Seaweed (Ulva lactuca) contains bioactive compounds such as tocopherols, chlorophyll, phenols, flavonoids, vitamins such as vitamin B1, B2, B12 and vitamin C that can accelerate the wound healing process[10].

According to research by Putu et al., 2023 seaweed (Ulva lactuca) contains bioactive compounds that act as antioxidants, anti-inflammatory, antihyperlipidemic, antimicrobial, and antiviral, and has the ability to maintain skin moisture. The content of phenol compounds, vitamin C, and alpha-tocopherol in sea lettuce provides benefits as an antioxidant that protects the body and skin from free radical damage. Based on this, this study aims to evaluate the potential antioxidant activity and antiradiation protection of Ulva lactuca extract-based cream[11].

The aim of this study was to determine the effect of seaweed (Ulva lactuca) hydrogel on cut wounds, as well as determining the extent to which the extract has properties to reduce inflammation, and accelerate tissue regeneration in wounds[12]. In addition, this study also aimed to assess the potential of seaweed (Ulva lactuca) extract as an alternative traditional treatment for wounds and observe the skin histopathology of Rattus norvegicus rats by examining the number of fibroblasts and re-epithelialization.

MATERIAL AND METHOD

This study used an experimental design with a post test control group design. This research was approved by the Prima Indonesia University Health Research Ethics Commission (071/KEPK/UNPRI/X/2023) and carried out at the

Pharmacology Laboratory of the University of North Sumatra and the Anatomical Pathology Laboratory of RSU Royal Prima from February to March 2024.

This study used white rat test animals (Rattus norvegicus) which were divided into six treatment groups. The purpose of the study was to evaluate the effect of seaweed (Ulva lactuca) extract concentration in wound healing, with three different doses (5%, 10%, and 15%) as treatment groups, as well as two control groups: positive control using bioplasentone and negative control (wound without treatment).

Tools and Materials

The tools used in this research are scalpel and surgical scissors, microscope, rotary evaporator, shaver, pestle/stamper and mortar. The materials used in this study are seaweed extract (*Ulva lactuca*), HE staining, 10% formalin, ketamine HCL-xylazine, xylol, PBS pH 7.4.

Seaweed Leaf Extract

Seaweed extract was obtained through maceration method. Previously, the seaweed was washed with running water and left overnight to dry. After that, the seaweed was cut into small pieces and crushed into powder[13]. The seaweed powder was then soaked in 96% ethanol for 24 hours, with occasional stirring, to dissolve the active compounds. After the soaking process, the solution was filtered to separate the pulp. The filtrate obtained was then evaporated using a rotary evaporator to produce a thick seaweed extract[14].

Formulation of Hydrogel Making

Manufacture of hydrogel is done by means of carbomer weighed as much as 3 grams dispersed into 50 ml of distilled water and stirred to form a basic gel. Next, add 0.2 grams of methyl paraben that has been dissolved in 96% ethanol, as well as glycerin, then stir until the mixture is homogeneous. Seaweed extract was then put into the hydrogel base and added 1 gram of trieatnolamine (TEA) then stirred until homogeneous. Added distilled water until the weight of the hydrogel becomes 100 grams[15].

Evaluation of Seaweed Extract (Ulva lactuca) Hydrogel Preparations

Evaluation of seaweed (Ulva lactuca) extract hydrogel preparations can be done through several tests aimed at assessing the quality, stability, and effectiveness of the preparation[16].

Organoleptical Test

Visual examination of nanoemulsion serum includes evaluation of color, aroma, consistency, and uniformity of the preparation[17].

pH Test

The pH test is carried out using a calibrated pH meter to measure the pH level of the serum at room temperature, with the aim of achieving a pH range of 5-7 which is in accordance with the pH of the skin, to ensure comfort and prevent irritation during use[18].

Homogeneity Test

The homogeneity test was visually performed by applying the hydrogel on three parts, namely top, middle, and bottom. The hydrogel was placed on a transparent glass and covered with an object glass to evaluate the clarity and presence of aggregates in the preparation[19].

Spreadability Test

The spreadability was measured using two glass plates, where one plate was given a millimeter block base to facilitate observation and measurement, while the other plate was used as a cover. A total of 1 gram of hydrogel was placed in the center of the glass plate, then covered with a cover glass and given a total load of 125

grams for 1 minute. After that, the diameter of the spread was calculated. Measurements were carried out in 3 replications[19].

Phytochemical Analysis of Seaweed (*Ulva lactuca*) Extract Hydrogel

Phytochemical analysis was performed to determine the type of secondary metabolites using[20].

Steroid/triterpenoid test: 0.5 mL extract of each sample was dissolved in 0.5 mL chloroform and added 0.5 mL anhydrous acetic acid. The addition of 1-2 mL of concentrated sulfuric acid will produce a purple or brownish ring on the terpenoid interface, while bluish green discoloration indicates the presence of steroids.

Flavonoid Test: 50 mg of extract is dissolved in 1-2 mL of ethanol and add 100 mg of magnesium powder and ten drops of hydrochloric acid. A color from orange-red to purplish red indicates the presence of flavonoids.

Alkoloid Test: 1mL of 2N HCL with 50 mg extract and 9 mL of water were mixed. After that, it was heated, filtered and tested with mayer reagent plus Bouchardt. There is a white precipitate after the addition of mayer reagent and a brownish orange precipitate on the addition of bouchant reagent indicates the presence of alkoloids.

Saponin Test: 50 mg extract was mixed with 10 mL of hot water and homogenized. There is a stable foam that lasts for 10 minutes and does not disappear after adding 1 drop of HCL 2N is formed.

Animal and Experimental Trials

The test animals were white rats (Rattus norvegicus) placed in plastic cages equipped with wire covers and husk mats[21]. The rats were divided into six treatment groups, each containing five rats in one cage[22]. Prior to treatment, the animals were adapted for 14 days to ensure their comfort. Each rat was given food and water freely (ad libitum) every day[23].

The groups were given different treatments: Group I was applied seaweed (Ulva lactuca) extract in hydrogel form at a dose of 5%, group II at a dose of 10%, and group III at a dose of 15%. Group IV was given bioplasentone as a positive control, group V was given no treatment as a negative control, and group VI consisted of rats that received no treatment at all as a normal control. The application was done twice a day, in the morning and evening, for 14 consecutive days[24]. The wound healing process in the rats was observed and assessed for 14 days after application of the seaweed (Ulva lactuca) extract hydrogel.

Histopathological Examination

Histopathology preparations were made using the paraffin method to observe the presence of inflammatory cells, fibroblast cells, and epithelium. Rat skin samples were taken and stained using Harris-hematoxylin eosin, then observed under a binocular light microscope with 100x and 450x magnification[25].

Data Analysis

Data analysis was performed to assess the progression of wound healing in the epidermis, dermis, and hypodermis areas by identifying the presence of inflammatory cells, fibroblasts, and epithelium[26]. The ANOVA test was used to compare means between multiple sample groups and test for differences in data means if more than six groups were involved. Decision-making based on the results of the ANOVA test was carried out with the criterion that if the sig value > 0.05, the data was considered normally distributed, while if the sig value < 0.05, the data was considered not normally distributed. Post-hoc analysis was performed to identify significant differences between groups.

RESULTS AND DISCUSSION

Phytochemical Screening

Phytochemical analysis of seaweed (Ulva lactuca) extract hydrogels revealed that they contained several bioactive compounds, including flavonoids, saponins and triterpenoids. However, this extract hydrogel did not contain tannin and alkaloid compounds, which are usually also found in other medicinal plants. These findings suggest that seaweed extract hydrogels have the potential to contain active compounds that may contribute to therapeutic effects, particularly in wound healing.

Evaluation Test of Seaweed Extract Hydrogel

Table 1. Organoleptical Test Results on Seaweed Hydrogel Extract Preparations

Organoleptic Test	Normal	F1 5% Result	F2 10% Result	F3 15% Result
Aroma	No odor	Characteristic Odor	Characteristic Odor	Characteristic Odor
Color	Clear	Faded Green	Green	Intense Green
Shape	Gel	Gel	Gel	Gel
Homogeneity	Homogeneous	Homogeneous	Homogeneous	Homogeneous

Based on the results of the study, seaweed extract (Ulva lactuca) hydrogels showed organoleptic test results which included aroma, shape, color, and homogeneity. The three hydrogel preparations, namely F1, F2, and F3, have similarities in the distinctive aroma and shape of the gel. However, differences were found in the color of the preparation. F1 hydrogel has a faint green color, F2 is green, and F3 is intense green.

Table 2. Results of pH Measurement on Seaweed Hydrogel Extract Preparations

Preparations	pH Measurement Results			
	Repetition			Mean±STD
Normal	6.42	6.41	6.39	6,40±0,33
F1: 5%	6.38	6.38	6.37	6,37±0,66
F2: 10%	6.36	6.34	6.33	6,34±0,33
F3: 15%	6.30	6.31	6.30	6,30±0,33

The results of pH measurements on the various hydrogel preparations tested showed pH values that were quite stable and within the safe range for use on the skin. In normal preparations, the measured pH values were 6.42, 6.41, and 6.39 with a mean ± STD of 6.40 ± 0.33. For the F1 preparation with a concentration of 5%, the pH measurement results were 6.38, 6.38, and 6.37, with an average ± STD of 6.37 ± 0.66, indicating a slightly lower pH but still within a safe range. In preparation F2 with a concentration of 10%, the measured pH values were 6.36, 6.34, and 6.33, with an average ± STD of 6.34 ± 0.33, which was slightly lower than F1. Whereas in preparation F3 with a concentration of 15%, the pH measurements showed values of 6.30, 6.31, and 6.30, with an average ± STD of 6.30 ± 0.33, which was the lowest pH value among all preparations. Overall, the pH values of all hydrogel preparations were within the range of 6.30 to 6.40, which is very compatible with the pH of human skin, which ranges from 4.5 to 7.5, making these preparations safe for topical application without the risk of irritation.

Table 3. Results of Evaluation of Spreadability Test on Seaweed Hydrogel Extract Preparations

Spreadability Test	0 grams	100 grams	150 grams
Normal	3.2 cm	3.4 cm	4.0 cm
F1: 5%	3.7 cm	4.6 cm	4.7 cm
F2: 10%	3.6 cm	4.6 cm	4.8 cm
F3: 15%	3.7 cm	4.5 cm	5.3 cm

The results of the spreadability test on the seaweed (Ulva lactuca) extract hydrogel preparation showed that the spreadability of the preparation increased with the addition of the load. In the normal preparation, with a load of 0 grams, the

recorded spreadability was 3.2 cm, and with a load of 100 grams and 150 grams, the spreadability increased to 3.4 cm and 4.0 cm, respectively. For preparation F1 (5% seaweed extract), the spreadability at 0 gram load was 3.7 cm, which was slightly greater than normal. At a load of 100 grams, the spreadability increased to 4.6 cm, and with a load of 150 grams it reached 4.7 cm, indicating that this preparation has better spreadability than the normal preparation. Preparation F2 (10%) showed a spreadability of 3.6 cm at 0 gram load, 4.6 cm at 100 gram load, and 4.8 cm at 150 gram load. Whereas in preparation F3 (15%), the spreadability at 0 gram load was 3.7 cm, increased to 4.5 cm at 100 gram load, and reached 5.3 cm at 150 gram load, which was the highest spreadability value among all preparations. The results of the spreadability test showed that increasing the concentration of seaweed extract (Ulva lactuca) can increase the spreadability of hydrogels, with preparation F3 (15%) showing the best results.

Length of Wound Healing

Wound healing observations were made for 14 days, with measurements taken on days 1, 3, 6, 9, 12, and 14. The decrease in wound length is shown in Table 4 below:

Table 4. Results of Wound Observations in White Rats

Group	Day 0	Day 3	Day 6	Day 10	Day 14	Average
P1: 5%	15.38	10.9	7.74	4.7	2.36	8.22
P2: 10%	15.52	11.42	10.42	8.74	7	10.62
P3: 15%	15.72	12.92	10.9	9.76	6.24	11.11
P4	15.74	11.88	7.7	6.12	3.38	8.964
P5	15.44	11.84	11.76	8.96	7.58	11.12
P6	0	0	0	0	0	0

The results from the table show the progression of wound healing in mice treated with seaweed extract (Ulva lactuca) at various concentrations. On Day 0, all groups had similar wound sizes. During observation, the 5% hydrogel-treated group (P1) showed the fastest healing, with the smallest wound size (2.36 mm) on Day 14. The 10% (P2) and 15% (P3) groups also showed a decrease in wound size, albeit slower, with wound sizes of 7 mm and 6.24 mm on Day 14, respectively. The negative control group (P5) showed slower healing (11.12 mm), while the untreated group (P6) showed no healing.

Table 5. One-way Anova Test

ANOVA		
Group	Sig.	Description
5% 10% 15% K+ K-	0,000	Significantly Different Data

The results of the ANOVA test on the Normality test using the Shapiro - Wilk Test obtained $p > 0.05$ so that the data is considered normally distributed. Then proceed to the homogeneity test and obtain results in the form of $p < 0.05$, which means that the variation between data groups is significantly different or the homogeneity test is not fulfilled.

Table 6. Post Hoc Test

Multiple Comparisons			
Games-Howell			
Group	Comparison Group	Sig.	Description
5%	10%	0,001	Significantly Different
	15%	0,01	Significantly Different
	K+	0,005	Significantly Different
	K-	0,003	Significantly Different
10%	5%	0,001	Significantly Different
	15%	0,271	No difference
	K+	0,048	Significantly Different
	K-	0,011	Significantly Different
15%	5%	0,01	Significantly Different
	10%	0,271	No difference
	K+	0,532	No difference
	K-	0,064	No difference
K+	5%	0,005	Significantly Different
	10%	0,048	Significantly Different
	15%	0,532	No difference
	K-	0,502	No difference
K-	5%	0,003	Significantly Different
	10%	0,011	Significantly Different
	15%	0,064	No difference
	K+	0,502	No difference

The table above shows that the average of the 5% treatment group with other treatment groups is significantly different. The average of the 10% and 15% treatment groups is not significantly different while the other groups are significantly different. The average of the 15% and 5% treatment groups is significantly different while the other treatment groups are not significantly different. The average of the K+ treatment group of 5% and 10% is significantly different and the 15% and K- treatment groups are not significantly different. The average of the K- treatment group against 5% and 10% is significantly different and the 15% and K+ treatment groups are not significantly different.

Skin Histopathology Analysis

Skin histopathology observations were made by assessing the parameters of changes in the skin, including epithelial thickness, the number of inflammatory cells, and collagen tissue.

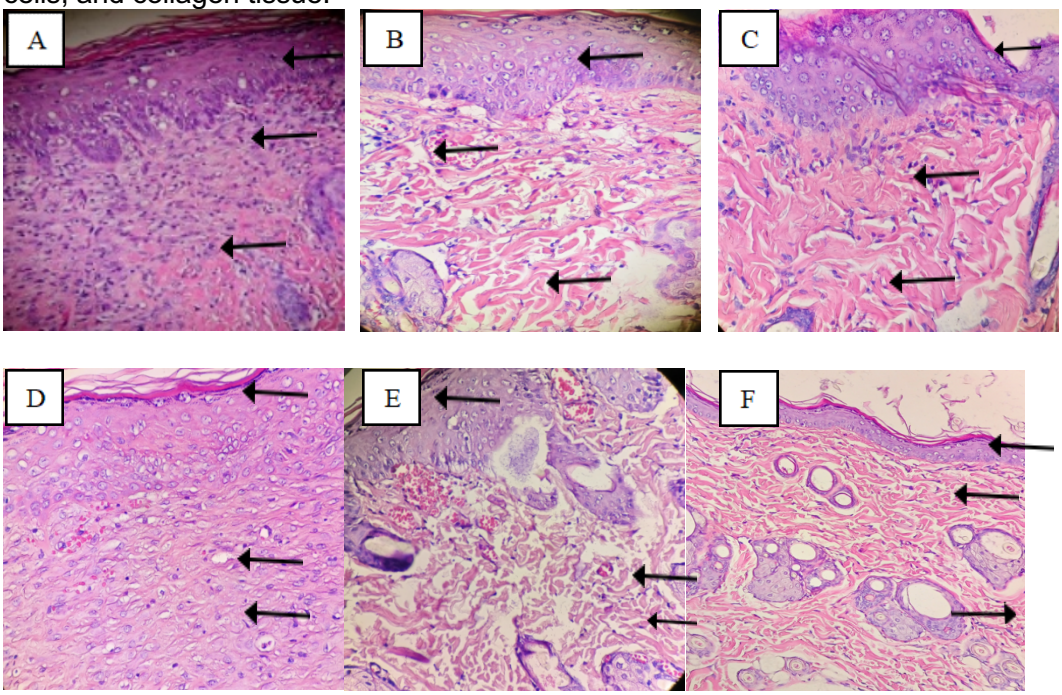

Figure 1: Skin histopathology analysis.

A: 5% seaweed extract hydrogel showing epithelial tissue lined by stratified squamous cells with moderate epithelial thickening. There were a moderate number of inflammatory cells as well as collagen network formation of about 50%. B: 10% seaweed extract hydrogel showed epithelial tissue lined by stratified squamous cells with moderate epithelial thickening, moderate presence of inflammatory cells, and collagen tissue formation of about 50%. C: 15% seaweed extract hydrogel showed a layered network of squamous cells with moderate epithelial thickening, moderate presence of inflammatory cells, and collagen network formation of 70%. D: bioplacenton (Positive Control) showed a layered tissue of squamous cells with moderate epithelial thickening, a moderate number of inflammatory cells, and collagen tissue formation of about 50%. E: untreated wounded rats (Negative Control) showed a layered tissue of squamous cells with moderate epithelial thickening, moderate presence of inflammatory cells, collagen network formation of about 50%, and interstitial hemorrhage. F: Treated normal mice showing stratified squamous cell layer tissue and the presence of hair follicles, sebaceous glands, and collagenous tissue.

Discussion

Phytochemical test results showed that seaweed (Ulva lactuca) extract hydrogels contain flavonoids, saponins, and triterpenoids. These compounds have been shown to have antioxidant and anti-inflammatory activities that support the wound healing process. Flavonoids can reduce oxidative stress and increase collagen synthesis, while saponins have the ability to increase cell permeability and accelerate tissue healing. Meanwhile, a 5% concentration of seaweed extract showed the most significant healing effect, which may be due to the balance between a sufficiently high concentration of active compounds and optimal bioavailability. The same results were also obtained from research (sanget et al, 2018) stating that seaweed (Ulva lactuca) is known to contain bioactive compounds such as tocopherols, chlorophyll, phenols, flavonoids, tannins, and alkaloids that are beneficial in the inflammatory healing process. However, the results of phytochemical examination showed that seaweed (Ulva lactuca) only contains flavonoids, saponins, and triterpenoids, while tannins and alkaloids were not detected in the extract [27].

Based on the results of organoleptical evaluation tests on seaweed extract hydrogels, F1, F2 and F3 hydrogel preparations have the same aroma and shape, and the color of F1 is pale green, F2 is green and F3 is solid green. This is in line with research conducted by (Nada Septiawan et al., 2020), which has a distinctive aroma. The green color of Ulva lactuca extract hydrogel is caused by chlorophyll-a contained in green algae (Ulva lactuca). The content of chlorophyll-a in green algae is highly dependent on temperature, altitude and microorganisms contained in the habitat of the waters [28].

The spreadability test on the hydrogel is carried out to determine how well the preparation spreads on the skin surface which affects the absorption of the drug and the speed of releasing the active substance in the application. A preparation that has a spreadability that is said to be good when it is easy to spread and its use is comfortable. The spreadability of topical preparations in accordance with the requirements is 5-7cm[28]. Based on this study, it was found that the spreadability of F1 0gr, 100gr and 150gr preparations was 3.7cm, 4.6cm and 4.7cm. F2 0gr, 100gr, 150gr preparations are 3.6cm, 4.6cm and 4.8cm. While in F3 0gr, 100gr and 150gr in the form of 3.7cm, 4.5cm and 5.3cm. So it can be said that the seaweed extract hydrogel (Ulva lactuca) used by researchers does not have good spreadability.

In the One Way ANOVA test, a p value of <0.05 was obtained, which means that the null hypothesis is rejected and there is a significant difference between the group means. Furthermore, the Post Hoc test was conducted to determine pairs of groups that were significantly different. The results of the Post Hoc test showed that the 5% treatment group was significantly different from the other treatment groups.

The means of the 10% and 15% treatment groups were not significantly different, but both were significantly different compared to the 5% treatment group. The 15% treatment group also showed significant differences with the 5% treatment group, while the differences with the other treatment groups were not significant. In addition, the positive control group (K+) showed significant differences compared to the 5% and 10% treatment groups, but not significantly different from the 15% treatment group. The negative control group (K-) was significantly different from the 5% and 10% treatment groups, but not significantly different from the 15% treatment group and the positive control (K+).

From the results of the study using the SPSS test, it was found that seaweed (Ulva lactuca) extract hydrogels with concentrations of 5%, 10%, 15%, and bioplasentone (K+) showed a positive effect in wound healing in white rats, while the negative control group (K-) which was not treated showed no improvement. The 5% concentration of seaweed extract hydrogel showed the most significant healing effect, as seen from the wound improvement on day 3, day 6, and day 14, with the wound showing complete healing.

The administration of plant extract hydrogel preparations can accelerate wound healing by shortening the inflammatory phase, so that the proliferation phase and wound healing can take place more quickly. Research by Putu Dea Anantarini et al. (2022) showed that several metabolite compounds, such as flavonoids, terpenoids, alkaloids, saponins, triterpenoids, and tannins, play an important role in regulating the inflammatory phase. Flavonoids, for example, stimulate the release of pro-inflammatory cytokines and growth factors such as transforming growth factor (TGF), platelet-derived growth factor (PDGF), fibroblast growth factor (FGF), and epidermal growth factor, which play a role in the wound healing process. Then, inflammatory cells such as neutrophils, macrophages and lymphocytes will migrate to the wound area. Neutrophils will clean microorganisms and cell debris in the wound and produce chemicals such as proteases and reactive oxygen species (ROS) that help in the wound cleaning and healing process[29].

Histopathologic examination of white rat skin treated with seaweed extract hydrogel (Ulva lactuca) at various concentrations showed changes in epithelial thickness, inflammatory cells, and collagen formation. At concentrations of 5%, 10%, and 15%, there was moderate epithelial thickening, many inflammatory cells, and increased collagen formation. This is in line with research by Windyaswari et al. 2019 which showed that seaweed extract can accelerate wound healing by stimulating epithelial growth, reducing inflammation, and repairing collagen tissue[30]. In the positive control group (Bioplasenton), the results also showed similar improvements, while in the negative control group where no treatment was given, only inflammation and little collagen formation were found. The 15% concentration showed good improvement, although no other studies have used the same concentration.

CONCLUSION

This study showed that seaweed (Ulva lactuca) extract hydrogel at a concentration of 5% proved effective in accelerating wound healing in white rats (Rattus norvegicus). This can be seen from the decrease in inflammation and the increase in collagen formation which is more significant than the other treatment groups. At concentrations of 10% and 15%, and bioplasentone also gave good results, no significant differences were found between the groups. Therefore, this study suggests that 5% concentration is the optimal choice. Further research is needed to test the stability of this hydrogel formulation and evaluate its effectiveness in human clinical trials.

AUTHORS' CONTRIBUTIONS

ST: Conceptualization, Methodology, Writing - Review & Editing; RI: Review & Editing; FMW: Review & Editing; All authors contributed equally in every stage of the research process.

ACKNOWLEDGEMENT

I would like to thank the Head of the Pharmacology Laboratory of the Faculty of Pharmacy, University of North Sumatra and the Head of the Anatomical Pathology Laboratory of Royal Prima Medan Hospital, for all their support for this research.

FUNDING INFORMATION

This research is self-funding

DATA AVAILABILITY STATEMENT

The utilized data to contribute to this investigation are available from the corresponding author on reasonable request.

DISCLOSURE STATEMENT

The views and opinions expressed in this article are those of the authors and do not necessarily reflect the official policy or position of any affiliated agency of the authors. The data is the result of the author's research and has never been published in other journals.

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